FLAVONOID OXIME COMPLEX SYNTHESIS WITH METAL IONS IN THE TREATMENT OF OXIDATIVE STRESS

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ABSTRACT

Oxidative stress is a phenomenon that results in cell and tissue damage in the human body [1]. In oxidative stress, formation of reactive oxygen and nitrogen species (ROS and RNS) increases and weakens body antioxidant defense and protection, subsequently causing DNA damage, lipid peroxidation, protein modification and other effects, all responsible for a number of diseases, including cancer, cardiovascular disease, diabetes, atherosclerosis, neurological disorders (Alzheimer's, Parkinson's disease), and chronic inflammation. The antioxidant activity of flavonoids and their derivatives, has shown great research interest in recent years, further envisioning to gain strength through metal ion complexation. In fact, it has been proven that certain metal ions have a positive impact on the human body's immune defense, due to metal-regulatory mechanisms operating in cells [2]. In that respect, the oxime functional group is considered to strengthen the biological efficiency of a flavonoid molecule, thereby potentially enhancing cell protection and antioxidant activity [3]. Concurrently, metal complexes of flavonoids appear to exhibit intensified antioxidant properties compared to the nascent form of flavonoid. However, this is not happening in every case of flavonoid-metal ion chemical reactivity and complexation [4]. To resolve the importance of flavonoid derivatization and subsequent metal ion complexation, providing enhanced biological activity and antioxidant potency, research work was launched in our Lab to include both flavonoids and physiologically relevant metals in complex species. To that end, the undertaken work has focused on the synthesis of complexed naringin oxime with an physiological metal ion (e.g. Zn(II)). To achieve this goal, binary and ternary systems involving naringin oxime, metal ions, and N,N'-terminal aromatic chelators (e.g. 1,10-phenanthroline) were investigated. Moreover, in vitro studies in neuronal cell cultures (N2a58 and SHSY5Y) showed high bioavailability of the new flavonoid derivative and its metal complex form(s), with enhanced antioxidant potential. The collective data exemplify the improved physicochemical profile of the derivatized flavonoid and its metal forms, thereby meriting further exploration of their biological role as antioxidant agents in the treatment of human pathologies.

KEYWORDS: Oxidative stress, Flavonoids, Metal complexation, Naringin oxime, antioxidant activity

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